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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/487,032	06/07/95	SMITH D	GTN-001

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EXAMINER	
PORTNER, V	
ART UNIT	**PAPER NUMBER**
1641	26

DATE MAILED: 07/29/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant
08/487,032	Smith
Examiner	**Group Art Unit**
Portner	1641

☒ Responsive to communication(s) filed on *Jul 12, 1999*.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *113-195* is/are pending in the application.

Of the above, claim(s) *158-195* is/are withdrawn from consideration.

☒ Claim(s) *124* is/are allowed.

☒ Claim(s) *113-123 and 125-157* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☒ Claims *113-195* are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *5,6,7,10,*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Claim 103 has been canceled, new claims 113-195 submitted and are pending.

Election/Restriction

1. In response to the supplemental Preliminary Amendment submitted July 12, 1999 the election/restriction requirement has been set forth below.

2. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 113-157 are, drawn to compositions, immunogenic compositions and vaccines comprising said compositions comprising SEQ ID No 764, classified in class 530, subclass 350.

II. Claims 158-195 are, drawn to methods of treating and preventing infection, classified in class 424, subclass 234.1.

3. The inventions are distinct, each from the other because of the following reasons:

4. Inventions I and II are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the product as claimed can be used in a materially different process of using that product is useful in methods of detecting infection (antibodies), in methods of purifying antibodies (affinity chromatography) and in the production of molecular image polymers.

5. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification and have acquired a separate status in the art because of their recognized divergent subject matter, restriction for examination purposes as indicated is proper.

6. During a telephone conversation with Ms. Amy Mandragorous on July 18, 1999 a provisional election was made with traverse to prosecute the invention of Group I, claims 113-157. Affirmation of this election must be made by applicant in replying to this Office action. Claims 158-195 are withdrawn from further consideration by the examiner, 37 CAR 1.142(b), as being drawn to a non-elected invention.

Drawings

7. This application has been filed with informal drawings which are acceptable for examination purposes only. Formal drawings will be required when the application is allowed.

Information Disclosure Statement

8. The information disclosure statement filed April 1996, October 1996, May 1997 and April 14, 1999 have been considered as to the merits prior to first action.

Election/Restriction

9. Applicant's election without traverse of Group I, SEQ ID No. 764 in Paper No. 23 is acknowledged.

10. Applicant states that upon indication of allowable subject matter that an additional species will be searched (page 2, paragraph 3, under "Remarks"). This statement is not reflective of the election made of record on paper number 20, which was not an election of species restriction/election but the election of a single independent and distinct invention. Therefore, with only a single invention remaining in claims of the instant Application, the examiner will examine SEQ ID NO 764 as directed by Applicant.

Please Note: the word "recombinant" is being read as a process step which can be carried out in nature or in the laboratory and not a state of purity.

Claim Rejections - 35 U.S.C. § 101

11. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

12. The claimed invention of Claims 113-123, 132-139,149,150, 152, 153,155 156, in so far as they recite "or recombinant polypeptide" is directed to non-statutory subject matter wherein recombination takes place in nature and would therefore result in the production of

recombinant polypeptides. Akopyanz is cited to show that diversity among isolates of Helicobacter pylori, and recombination and expression of polypeptide naturally occurs in nature. This rejection could be obviated by amending the claim to recite a phrase which defines the invention as a purified product using language consistent with the teachings of the specification.

Please Note: the phrase "pharmaceutically acceptable carrier" is being read as a component of a composition for administration to an animal which serves or may serve as a host to Helicobacter.

Claim Rejections - 35 U.S.C. § 112

13. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

14. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

15. Claims 148-157 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for claims limited compositions comprising SEQ ID No 764 (the elected invention), a method of purifying or synthesizing said SEQ ID NO 764, a method of culturing Helicobacter pylori, recombinantly

produced Helicobacter antigen, DNA, vectors, host cells comprising the nucleic acid sequence which encodes SEQ ID No 764, does not reasonably provide enablement for a vaccine or compositions comprising an effective amount of an immunogenic composition. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The claim recites a vaccine comprising an effective amount of a polypeptide of Helicobacter pylori comprising SEQ ID NO 764. The specification teaches compositions comprising this polypeptide with an intended use for parenteral or oral administration, and teaches that the composition may be administered by **any** conventional route in use in the field of vaccines and may be administered in a single dose or in more than one dose over a given interval. The term "vaccine" encompasses the ability of the specific polypeptide antigen to induce protective immunity, in the case of the instantly claimed invention, the protection or prevention of infection would be against pathogenic *Helicobacter*.

The specification does not provide substantive evidence that the claimed vaccine is are capable of inducing protective

immunity for prevention or treatment of H. pylori, especially using only an antigenic preparation without co-administration of said preparation together with a mucosal adjuvant, and more specifically, no immunogenic compositions have been shown to evidence characteristics which would afford a host protection against infection or to aid in the treatment of Helicobacter infection. The art recognized standard for the determination of Helicobacter pylori infection is endoscopy and evaluation of tissue samples for the presence or absence of Helicobacter (see Buck et al, 1986). It is the examiner's position that a urease test is not directly indicative of, nor is it the art recognized standard for the evaluation of a method for the treatment or prevention of Helicobacter infection. Data obtained from challenge experiments must demonstrate an art recognized standard of improvement over the control in order for the composition to be considered as being useful for treatment or prevention of infection. This information is essential for the skilled artisan to be able to use the claimed composition (vaccines) for their intended purpose of preventing *Helicobacter* infections. Without this demonstration, the skilled artisan would not be able to reasonably predict the outcome of the administration of the

claimed vaccines, i.e. would not be able to accurately predict if protective immunity has been induced.

The prior art teaches that Helicobacter pylori vaccines are unpredictable, specifically, in the type of effect they will have on preventing or treating infection; the ability to reasonably predict the capacity of a single bacterial immunogen, to induce protective immunity is problematic. In HP WORLD-WIDE, a publication from Brocades Pharma BV Leiderdorp, The Netherlands, February 1992, data was presented stating that immunization does not appear promising. Parenteral immunization of specific pathogen free mice with *H. felis* gave no protection against gastric colonization; previous oral infection only delayed colonization (Heap,K, Australia). The article also taught that "although intra-peyers patch immunization of killed *H. pylori* in rats shows that the gut mucosa can mount a vigorous immune response, oral immunization with either live or killed bacteria induced no significant serum or salival antibody response (Dunkley, M, Australia). Blaser also warned that because of the possible autoimmune component of the disease the wrong vaccine could actually make things worse."

Unfortunately, the vaccine art is replete with instances where even well characterized antigens that induce an in vitro

neutralizing antibody response fail to elicit in vivo protective immunity. See Boslego et al. wherein a single gonococcal pillin protein fails to elicit protective immunity even though a high level of serum antibody response is induced (page 212, bottom of column 2). Accordingly, the art indicates that it would require undue experimentation to formulate and use a successful vaccine without the prior demonstration of vaccine efficacy.

From the specification it is clear that Applicant has identified an antigenic polypeptide which results in an reacting with an antibody and could be easily produced by methods known in the art of protein chemistry but it is not clear that the polypeptide results in prevention of infection and disease. No art recognized *in vitro* or *in vivo* models are shown in which protection is produced from the instantly claimed invention. It is clear the polypeptide is immunogenic but it is not clear that the composition would result in prevention of infection or disease. No examples containing the missing information are shown.

It is known it the art that vaccines convey protection from infection and disease. Rappuoli et al (European Journal of Gastroenterology and Hepatology, 1993, Vol.5, (suppl. 2) pages 576-578) teach that development of a vaccine against *Helicobacter pylori* would involve four major steps:

1) identification of the factors required for virulence;

2) large-scale production and characterization of the virulence factors;

3) development of appropriate animal models to test the virulence and immunogenicity of the molecules identified; and

4) identification of the type of immunity able to prevent infection and disease.

Given the lack of guidance on how to obtain the desired effect using the claimed vaccine in a method of treating or preventing *H. pylori* infection, and in light of the teachings of the prior art which teaches that vaccines comprising Helicobacter antigens are unpredictable in methods of treating or preventing infection the skilled artisan could not make and use the claimed invention. No evidence is of record showing that **any** composition comprising SEQ ID 764 could confer the desired and claimed effect. No working examples are shown which convey the missing information. Therefore, the skilled artisan could not use **any** Helicobacter composition comprising *H. pylori* polypeptide SEQ ID No 764 to obtain the desired effect of preventing or treating infection without undue experimentation.

16. Claims 113-119,121-123, 132-139, 150, 153, 156 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The recitation of the word

"BLASTP" does not evidence original descriptive support in the specification and is therefore considered to be new matter. The phrase "percent sequence identity " also does not evidence original descriptive support in the specification and is therefore considered to be new matter. If there is specific support for these terms the examiner requests that Applicant point out support for these limitations. The use of the words "homology" and "homologous" are used throughout the specification.

17. Claims 113-123, 125-141 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. As the instant specification is clearly enabled and provides written descriptive support for SEQ ID No 764, no specific isolated or recombinant polypeptides which share 60%,70%,80%,90%,95%,98% or 99% sequence identity evidence original descriptive support in the instant specification. Compositions comprising specific immunogenic polypeptides which comprise any 5-100 consecutive amino acids are not taught in such a way as to define an effective amount of immunogenic polypeptide as the administration of SEQ ID NO 764 does not evidence original descriptive support in the instant specification. **The claimed immunogenic polypeptides do not consist of SEQ ID No 764** but portions of the SEQ ID are included in a larger immunogenic polypeptide as now claimed. No specific immunogenic polypeptide, which are not immunogenic fragments of the recited SEQ ID No 764, are described. The portions of SEQ ID NO 764 which are used in the formulation of the claimed immunogenic

polypeptides need not be immunogen portions of SEQ ID No 764. Therefore the immunogenic polypeptides as defined in the claims are not taught in the instant specification such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

18. Claims 113-119,121-123, 132-139, 150, 153, 156 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the specific amino acid sequences and their corresponding nucleotide sequences, vectors, host cells, methods of making a protein and methods of inducing an immune response using polypeptides, does not reasonably provide enablement for any polynucleotide which is homologous or a derivative to the recited sequences. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The specification is not enabled for amino acid sequences which evidence a percent identity or homology to of the claimed SEQ ID NO 764 which differs from that sequence.

Homologs and derivatives of the instant specification are obtained through the deletion, substitution or insertion of nucleic acids into the polynucleotide sequence which encodes SEQ ID NO 764, the specific locations where these changes can be made so the character of the encoded polypeptide is maintained are not taught. The claimed polypeptides which have a percent identity

with SEQ ID NO 764 would therefore evidence changes in the amino acid structure. In light of this fact, Thomas E. Creighton, in cited for what he teaches in his book,"Proteins: Structures and Molecular Properties, 1984",(pages 314-315) with respect to how variation of the primary structure of a protein can result in an instable molecule. He teaches that a single amino acid change can cause a mutant hemoglobin to have lower stabilities due to any of several causes:

1) alteration of close-packing of the interior; loss of one group that normally participates in a hydrogen bond or salt bridge;

2) the introduction of a charged or polar group into the interior or the insertion into a helical region of a Proline residue, which must distort the alpha-helix;

3) while sometimes radical changes of surface groups, even introduction of a non-polar side chain- have no great effect on stability.

Thomas E. Creighton, in his book "Protein structure: A Practical Approach, 1989; pages 184-186" teaches that present day site directed mutagenesis of a gene allows any amino acid in a protein sequence to be changed to any other, as well as introducing deletions and insertions. The reference goes on to

teach that it is difficult to know which amino acid to change and which is the best residue to substitute for the desired functional and structural effect.

Nosh, Y. et al in "Protein Stability and Stabilization through Protein Engineering, 1991" (chapter 7, page 197, second paragraph) adds support to Thomas E. Creighton, by teaching that results so far accumulated on the stability and stabilization of proteins appear to indicate that the strategy for stabilizing proteins differ from protein to protein and that any generalized mechanisms for protein stability have not yet been presented.

The construction of a polypeptide which evidence a percent identity or homology and is produce through changes in **any** location, would not predictably result in a stable polypeptide molecule. No working examples are shown containing the missing information. Without such information, one of skill in the art could not predict which deletions, substitutions or insertions or any combination thereof would result in the desired stable, active polypeptide. It is unclear to one skilled in the art what sequences are embraced by a claim which is based on a specification which lacks the algorithm and parameters used to determine percent identity for the now claimed polynucleotide which encodes homologs and derivative polypeptides because the specification is non-enabling, since one skilled in the art would not be able to make and use those sequences without undue experimentation.

19. Claims 113-119,121-123, 132-139, 150, 153, 156 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

20. Claims 113-119,121-123, 132-139, 150, 153, 156 are indefinite due to phrases "percent sequence identity with SEQ ID No 764" and "is determined by the BLASTP algorithm". The term "BLASTP" does not appear in the specification. At page 63, paragraph 2, reference to a BLAST program is recited but not the BLASTP program, and what is intended by a term that is not recited in the specification is not clear. The specific parameters and gaps used in running of the program are not disclosed and therefore the claimed polypeptide is not clearly defined and is therefore vague and indefinite. The phrase "percent sequence identity with SEQ ID No 764" is defined in terms of % homology or homologous to the recited sequence. The recitation of the phrase "percent sequence identity" was not specifically defined in the specification. If the claims which now recite "percent sequence identity " are read as "percent sequence homology with SEQ ID No 764 in connection with a recited amino acid sequence is vague and indefinite in the absence of a clear description or definition of what the term means. Sequence homology between two sequences has no common meaning within the art. Without a clear and unambiguous description of how to do a comparison to determine whether two sequences are homologous, the metes and bounds of the claims cannot be determined. Therefore, the claims do not distinctly claim Applicant's invention.

21. Claims 120-123, 132,133,134,135, 149,152 and 155, 125 and 126 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claims 125-131 do not require that the immunogenic portion of the claimed immunogenic polypeptide be from the recited SEQ ID 764; the meets and bounds of the claimed invention is vague and indefinite as the claimed portion of the sequence need not be an immunogenic fragment of SEQ ID NO 764.

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b. Claims 120-123, 132,133,134,135, 149,152 and 155 recite the phrase "hybridizes under stringent conditions to the complement of **a nucleotide sequence** encoding SEQ ID No 764"; what the nucleotides sequence is not clear as it can be *any nucleotide sequence*, of *any length*, *under any type of stringent conditions* which will hybridize with SEQ ID No 764. Therefore the claimed invention is vague and indefinite as the meets and bounds of the claim are not defined.

c. Claims 126-131,140,141, 142-148, 154,157 recite the phrase "at least about"; what is intended is not clear. For example: "at least about 5" could be read to mean 5 and above or 3 or 4 or 5 and above. The recitation of this phrase is not defined in the specification and the recitation of this limitation does not distinctly claim applicant's invention.

d.Claims 126-131 and depend from claim 125 recite limitations which lack antecedent basis in claim 125. For example, claim 126 recites "of claim 125 **comprising at least about 10 consecutive amino acid residues** of SEQ ID No 764". As claim 125 comprises an isolated

polypeptide of only 5 amino acids of SEQ ID No 764, limitations which set forth isolated polypeptides of greater than 5 amino acids do not find antecedent basis in claim 125.

e. Claims 132-140 are vague and indefinite for the recitation of the phrase "an isolated polypeptide". The claimed invention is a fusion protein operably linked to an additional amino acid sequence but it is not clear how an isolated polypeptide, isolated from natural sources is also a fusion protein. The claim does not distinctly claim Applicant's invention.

f. Claims 152-157 recite the phrase "an effective amount". The amount is not clear as what the amount is effective for is not defined in the claims. The claimed invention is vague and indefinite as an effective amount is not clearly defined in the specification.

g. Claims 142-148 recite compositions which comprise immunogenic **polypeptides** wherein **at least one** of the polypeptides comprises at least about 10 consecutive amino acids of SEQ ID NO 764. What other immunogenic polypeptides are contained in the compositions is not distinctly claimed. The meets and bounds of the claim can not be determined.

Claim Rejections - 35 U.S.C. § 102

h. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

22. Claims 125,140 rejected under 35 U.S.C. 102(e) as being anticipated by Wang (US Pat. 5,476,765, filing date June 1992) or Duncan (EP-371818A).

Wang and Duncan (EP-371818A) disclose an immunogenic polypeptide which share 100% identity with 6 amino acids of SEQ ID No 764 for the diagnosis of HIV infection, which is biotinylated (Wang) (an additional amino acid sequence) wherein the disclosed immunogenic polypeptide comprises 16 and 20 amino acids, respectively and therefore anticipates the now claimed invention.

23. Claims 125,140 rejected under 35 U.S.C. 102(e) as being anticipated by Kjeldsen et al (1991).

Kjeldsen et al disclose an immunogenic polypeptide which share 100% identity with 6 amino acids of SEQ ID No 764 wherein the disclosed immunogenic polypeptide comprises 935 amino acids, and therefore comprises an additional amino acid sequence. The reference anticipates the now claimed invention.

24. Claims 125,126, 140 rejected under 35 U.S.C. 102(a) as being anticipated by Davies et al (May 11, 1994).

Davies et al disclose a nucleotide sequence which encodes a recombinant and isolated polypeptide which share 100% identity with 5 amino acids of SEQ ID No 764 and about at least 10 amino acids of SEQ ID No 764, wherein 8 is at least about 10 which was expressed as a fusion protein and therefore anticipates the now claimed invention.

25. Claims 125,126, 140 rejected under 35 U.S.C. 102(a) as being anticipated by Crowe et al (November 10, 1994).

Crowe et al disclose a nucleotide sequence which encodes a recombinant and isolated polypeptide which share 100% identity with 5 amino acids of SEQ ID No 764 and about at least 10 amino acids of SEQ ID No 764, wherein 8 is at least about 10 and therefore anticipates the now claimed invention.

26. Claims 125 and 140 are rejected under 35 U.S.C. 102(b) as being anticipated by Fahnestock (WO88/10306).

Fahnestock (WO88/10306) disclose a nucleotide sequence which encodes a recombinant and isolated polypeptide which share 100% identity with 5 amino acids of SEQ ID No 764 and therefore anticipates the now claimed invention.

27. Claims 125,126, 140 are rejected under 35 U.S.C. 102(b) as being anticipated by Fuchs et al (1991).

Fuchs et al disclose a nucleotide sequence which encodes a recombinant and isolated polypeptide which share 100% identity with 5 amino acids of SEQ ID No 764 and about at least 10 amino acids of SEQ ID No 764, wherein 8 is at least about 10 and therefore anticipates the now claimed invention.

28. Claims 125,126, 140 are rejected under 35 U.S.C. 102(b) as being anticipated by Axelos et al (1989).

Axelos et al disclose a nucleotide sequence which encodes a recombinant and isolated polypeptide which share 100% identity with 9 amino acids of SEQ ID No 764 which is about at least 10 amino acids of SEQ ID No 764. The disclosed immunogenic polypeptide comprises additional amino acids and therefore meets the claim limitations of claim 140. Axelos et al anticipates the now claimed invention.

29. Claims 120-123,132-135, 149,152, 155 are rejected under 35 U.S.C. 102(b) as being anticipated by Newman et al (1994).

Newman et al disclose a nucleotide sequence which encodes an isolated or purified recombinant polypeptide wherein the nucleic acid sequence share 76.923 sequence similarity and would

hybridize under stringent conditions to SEQ ID No 764 and therefore anticipates the now claimed polypeptide.

30. Claims 142-148 are rejected under 35 U.S.C. 102(e) as being anticipated by Czinn et al (US Pat.5,538,729).

Czinn et al disclose compositions comprising immunogenic polypeptides from Helicobacter and teach a method of oral immunization against *Helicobacter pylori* and a vaccine comprising Helicobacter polypeptides and an adjuvant, wherein the adjuvant is a mucosal adjuvant. The compositions evidenced a significantly enhanced immune response when a mucosal adjuvant, specifically cholera toxin, was used with the vaccine comprising Helicobacter. The compositions comprising isolated immunogenic polypeptides of Czinn would inherently comprise the instantly claimed polypeptide as the composition of Czinn comprised all the antigens present in a whole cell lysate of Helicobacter. If applicants contend that this is not the case, applicants are advised that the Office does not have the facilities for examining and comparing applicant's product with the prior art, and that the burden is on applicant to show a novel or unobvious

difference between the claimed method and the method of the prior art.

Allowable Subject Matter

31. The following is a statement of reasons for the indication of allowable subject matter: SEQ ID NO 764 is not taught or reasonably suggested by the prior art of record. The now claimed composition is being read as being isolated and purified from other Helicobacter pylori antigens and does not read on a whole cell lysate which has been isolated from cellular debris because the polypeptide would have been significantly purified in order to determine the now recited amino acid sequence SEQ ID NO. Claim 124 is allowed.

Conclusion

32. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

33. Bukanov et al (1994) is cited to show a cosmid library of Helicobacter pylori.

34. Alemohammad (US Pat 5,252,156) is cited to Helicobacter pylori antigens.

35. Calenoff (US Pat. 5,567,594) is cited to show a library of antigens for Heliocbacter pylori which are reactive with IgE.

36. Czinn et al (US Pat. 5,538,729) is cited to show vaccine compositions comprising Helicobacter polypeptides.

37.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ginny Portner whose telephone number is (703)308-7543. The examiner can normally be reached on Monday through Friday from 7:30 AM to 5:00 PM except for the first Friday of each two week period.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached on (703) 308-4027. The fax phone number for this group is (703) 308-4242.

The Group and/or Art Unit location of your application in the PTO will be changing February 7, 1998. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Vgp
June 28, 1999

James C. Housel 7/29/99

JAMES C. HOUSEL
SUPERVISORY PATENT EXAMINER